

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s) : Wyndham H. Wilson and Robert E. Witter
Serial No. : 08/178,463
Filed : January 6, 1994
For : **TAXOL TREATMENT OF LYMPHOMAS AND BREAST CANCER**
Group Art Unit : 1205
Examiner : Jerome Goldberg

HONORABLE COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

Box: AF

DECLARATION OF BRUCE A. CHABNER UNDER 37 C.F.R. § 1.132

Sir:

I, Bruce A. Chabner, M.D., declare that:

1. I am the Director, Division of Cancer Treatment, at the National Cancer Institute at the National Institutes of Health in Bethesda, Maryland. I have held this position for 13 years.

2. I hold the following degrees: A.B., Yale University, 1961; and M.D., Harvard University, 1965.

3. I have extensive knowledge and experience in the chemotherapy of neoplastic diseases and expertise in the various chemotherapeutic compounds and pharmaceutical drugs and agents that have been discovered, developed, and used clinically for the treatment of

cancers and tumors. In addition, I have conducted studies using a variety of chemotherapeutic agents to treat cancers and tumors both in experimental animals and in humans.

4. I have also contributed to the general and specialized scientific literature through my original writings, papers, and authorships in journals and reference and text books. In particular, I am a co-author of both a Section (i.e., Section XII, "Chemotherapy of Neoplastic Diseases") and a Chapter (i.e., Chapter 52, "Antineoplastic Agents") with Dr. Paul Calabresi in the textbook *The Pharmacological Basis of Therapeutics*, 1990, Eighth Edition, Eds., Alfred Goodman Gilman, M.D., Ph.D., Theodore W. Rall, Ph.D., D.Med (Hon.), Alan S. Nies, M.D., and Palmer Taylor, Ph.D., Pergamon Press, Inc., Maxwell House, Fairview Park, Elmsford, New York (also referred to as "Goodman and Gilman" herein).

5. I am making this declaration in support of the allowance of the above-identified patent application.

6. I am further making this declaration to point out and discuss the ambiguity which surrounds a general statement relating maximal doses of taxol as presented in the above-mentioned chapter of the Goodman and Gilman textbook. This statement is found on page 1239 in Goodman and Gilman's Chapter 52, entitled "Antineoplastic Agents", authored by Paul Calabresi and myself, under the description of the antimitotic agent "Taxol". It is my opinion and belief that this statement is ambiguous and vague due to the fact that there is no mention of the dosing schedule or regimen used to administer the stated doses of taxol, as discussed further hereinbelow.

7. In particular, the general statement of maximal taxol doses that appears on page 1239 in the last line of column 1 and continues to lines 1-2 of column 2 of the Goodman and Gilman textbook, reads as follows: "[m]aximal doses are 30 mg/m² per day for 5 days or 210 to 250 mg/m² given once every 3 weeks."

8. I am aware that this statement related to taxol doses and quoted in ¶ 7 hereinabove has been applied against the claims pending in the above-identified application (See. Office Action. 11/28/94. p. 3).

9. As a co-author of the information pertaining to taxol in Goodman and Gilman's Chapter 52 on antineoplastic agents, and as one having more than ordinary skill in the art, it is my opinion and belief that the statement concerning maximal taxol doses does not designate or disclose any information concerning the dosing schedule or regimen used to administer taxol, and does not signify that taxol is given by continuous infusion over 5 days. Indeed, there is absolutely no indication in this statement of the overall taxol dosing schedule used to administer the maximal doses of taxol to an individual for 5 days. By "taxol dosing schedule or regimen" I mean the procedure, mode, schedule, and route used to administer a dose or doses of taxol to an individual.

10. Because there is no indication of the dosing schedule or regimen used to administer the maximal doses of taxol as written in the brief description of taxol appearing at page 1239 of the Goodman and Gilman textbook, the taxol dosing schedule or regimen cannot be determined or inferred from the information provided in the description. Furthermore, there is no "standard assumption" made by those skilled in the art concerning the taxol dosing schedule, since no information about the schedule is stated. Consequently,

and with specific regard to the taxol doses stated in Chapter 52 of the Goodman and Gilman textbook, those skilled in the art do not assume that continuous infusion is used to administer these taxol doses for 5 days, unless the statement explicitly reports that continuous infusion is used.

11. It is my further opinion and belief, based on factual information known to me, that it is established and general knowledge among those skilled in the art that if a reference (or other drug dosage information) does not state or specify that a drug is given by infusion or by continuous infusion, then *those skilled in the art do not assume that the drug is given by infusion or by continuous infusion.*

12. Based on my knowledge and experience in this art, I maintain that unless an article or reference unambiguously states that continuous infusion is the dosing schedule or regimen used to administer a drug or therapeutic compound such as taxol, there is neither an implicit nor an explicit presumption among those skilled in the art that continuous infusion is used.

13. I declare further that all statements made in this Declaration are of my own knowledge and are true and all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated:

4/2/95


Bruce A. Chabner, M.D.